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# Renal Function after Partial Nephrectomy versus Radical Nephrectomy for Renal Cell Carcinoma: A Comparative Study

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#### **Abstract**

Background: Renal cell carcinoma (RCC) is the third most common malignancy of the genitourinary system characterized by lack of early warning clinical manifestations (asymptomatic) and late triad of symptoms (flank pain, hematuria, and palpable renal mass). It accounts for approximately 2-3% of the adult malignancy and 90% to 95% of neoplasms arising from the kidney. With the improvement in imaging technique, small and asymptomatic RCC is easily diagnosed and treated but advanced RCC is difficult to treat because its inherent resistance to conventional chemotherapy and radiotherapy. Objective: To compare the timedependent changes of estimated glomerular filtration rate (eGFR) after partial nephrectomy (PN) and radical nephrectomy (RN) for renal cell carcinoma (RCC). Type of study: Randomized controlled clinical trial. Place of Study: Department of Urology, BSMMU and Comfort Nursing Home (Pvt.) Ltd. Dhaka, during the period of June, 2018 to December, 2020. Methods: This prospective randomized controlled clinical trial study is conducted in the Department of Urology, BSMMU and Comfort Nursing Home (Pvt.) Ltd, Dhaka, From June, 2018 to December, 2020. Total 52 patients having renal cell carcinoma (<7cm) and normal contralateral kidney, available preoperative and postoperative serum creatinine and MDRD-eGFR measurements are included in this study, Preoperative MDRD-eGFR<30 ml/min/1.73m2 or serum creatinine level >1.5 mg/dl before surgery is excluded from this study. After detailed explanting about the nature of the study to the participants and with written consent, 52 patients are randomly allocated into two groups by lottery method. In group-A 26 patients are enrolled for partial nephrectomy (PN) and in group-B, 26 patients are enrolled for radical nephrectomy (RN). The enrolled patients are evaluated after surgical intervention under general anesthesia with different surgeons in two institutes by measuring serum creatinine and MDRD-eGFR postoperatively 1, 3, 7 days, and 3 monthly for one year. MDRD-eGFR declining is assessed from the preoperative value to the 1st post-operative value at the end of follow up. During follow up period, out of total 52 patients in both groups 1 patient in group-A and 2 patients in group-B did not come in regular follow up and one patient died in group-A So total 23 patients in each group are followed up after operation. **Results:** Demographic characteristics, BMI, pre- and post-operative symptoms and sign of the patients, most of the tumor characteristics (location, hydronephrosis and enhancement) are not statistically Significant in both groups but statistically significant changes are found in tumor size (p=0.004) and tumor type (p=0.013). There is no significant difference in pre-operative serum creatinine and eGFR in both groups but the time-dependent changes of eGFR after RN show plateau form initially and then gradually declining form the first post-operative day to the 12 post-operative months. In case of partial nephrectomy (PN), a lowest eGFR is observing in post-operative day 1 and gradually recovered to near pre-operative level for 12 months. The mean (±SD) eGFR decreased more significantly in RN (group-B 18.56 ml/min) than PN patients (group- A 6.31 ml/min) from pre-operative to 12 months after operation and shows statistically significant differences between and within both groups (p<0.001, <0.001 respectively). Conclusion: Time dependent changes of estimated glomerular filtration rate (eGFR) after partial nephrectomy (PN) is better than radical nephrectomy (RN) for renal cell carcinoma (RCC). Partial nephrectomy (PN) is therefore the better procedure for preservation of renal function.

Keywords: Demographic Characteristics, BMI, Radical Nephrectomy (RN), Renal Cell Carcinoma (RCC), Post-Operative Symptoms.



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#### INTRODUCTION

Renal cell carcinoma (RCC) is the most common malignancy of the kidney and accounts for about 2-3% of all adult neoplasms.[1] Overall, approximately 12 new cases are diagnosed per 100,000 population per year, with a male-tofemale predominance of 3:2. This is primarily a disease of older adults, with typical presentation between 50 and 70 years of age.<sup>[2]</sup> The incidence of renal tumors has risen over the last decades. Due to the progress in radiological imaging, the majority of renal tumors are detected incidentally (<50%) during diagnostic work-up for other patient complaints. The triad of symptom-flank pain, gross hematuria, and palpable mass only occur in the minority of patients (7-10%) and are usually a sing of locally advanced disease.[3] Radical nephrectomy (RN) has been standard treatment for any renal cell carcinoma (RCC) during the last 30 The role of open radical nephrectomy in the management of RCC has changed somewhat over the decade.[1] Although last nephrectomy (RN) has long been the standard treatment for renal cell carcinoma (RCC), many studies have been documented recently improved overall survival, better preservation of renal function, the safety and oncological efficacy of partial nephrectomy (PN) for RCC.[3] The current guidelines form the European Urology Association (EUA) and American Urology Association (AUA) have recommended PN for RCCs smaller than 4cm. Despite these recommendations, RN is still widely

performed for small tumors in individuals with a normal contralateral kidney.<sup>[4]</sup> Partial nephrectomy (PN) with resection of the tumor only was usually reserved for patients with solitary kidney, bilateral tumors or chronic kidney disease. It has become the standard of surgery for patients with solitary kidney, bilateral tumors or chronic kidney disease. It has become the standard of surgery for patients presenting with renal tumors <4 cm in size (cTla) with a healthy contralateral kidney due to good oncological long-term outcomes with a moderate perioperative complication rate. In selected cases PN is considered as alternative treatment for 4-7 cm sized renal tumors (cTlb). For renal tumors>7 cm in size (cT2a), PN can also performed safely in properly selected patients with good short-term functional and oncologic outcomes. Both RN and PN are therefore considered standard treatments for RCC and the main difference in outcome between these procedures is the preservation of renal function.<sup>[3]</sup> Renal function after surgery for RCC has usually been assessed by using serum creatinine (SCr.) level alone but SCr. is affected by factors affecting generation, including muscle mass and dietary intake. As a result, renal function tends to be overestimated in patients who are elderly or for some other reason have decreased muscle mass. Furthermore, it is difficult to evaluate SCr. level in both male and female patients because the normal ranges of serum creatinine differ between men and women. So, eGFR is the most accurate index for assessing



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renal function and the National Kidney Foundation Kidney Disease Outcome Quality Initiative (NKF KEOQI) guidelines recommended using estimated glomerular filtration rate(eGFR) with age, diabetes and hypertension.<sup>[5]</sup> In a study of 253 patients with RCC by Miyamoto et al.[6] Have assessed the renal function using the eGRR and investigated the time dependent changes of the eGFR after the operation and found postoperative eGFR≥60 ml /min is 23% and 57.6% in nephrectomy radial and partial nephrectomy respectively. The aim of this study is to evaluate the timedependent changes or renal function of the patents after RN and PN for RCC using MDRD equations estimating eGFR from measuring creatinine level pre-operatively and post-operatively 1,3,7 days, and 3 monthly for one year the Bangladeshi population and the result of this study will emphasize more in renal preserving procedure for eligible patients with RCC.

#### **Objective**

## General objective:

 To compare renal functional status after partial nephrectomy and radical nephrectomy for renal cell carcinoma.

### **Specific objectives:**

- To estimate serum creatinine among the patients undergoing partial nephrectomy and radical nephrectomy before operation.
- To estimate serum creatinine among the patients undergoing partial nephrectomy and radical nephrectomy after operation at different interval.

- To estimate eGFR among the patents undergoing partial nephrectomy and radical nephrectomy before operation.
- To estimate eGFR among the patients undergoing partial nephrectomy and radical nephrectomy after operation at different interval.
- To compare eGFR among the patients undergoing partial nephrectomy and radical nephrectomy after operation at different interval.
- To compare eGFR between partial nephrectomy and radical nephrectomy patients.

#### **MATERIALS AND METHODS**

<u>Type of study:</u> Randomized controlled clinical trail

<u>Study period:</u> June, 2018 to December, 2020.

<u>Study place:</u>Department of Urology, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Comfort Nursing Home (Pvt.) Ltd. Dhaka.

<u>Study population</u>:Patients having renal cell carcinoma (≤ 7cm) attending in the outpatient department of BSMMU hospital and Comfort Nursing Home (Pvt.) Ltd, Dhaka from June, 2018 to December, 2020 is included in this study and surgical intervention is done.

#### **Inclusion criteria:**

- 1. Age (35-75 years)
- 2. A solitary renal mass, size ≤ 7cm (cT1a, cT1b)
- 3. A radiographically normal contralateral Kidney

#### **Exclusion criteria:**

1. Patient with a preoperative serum creatinine level> 1.5 mg/dl.



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- 2. Patient with a preoperative glomerular filtration rate <30 ml/min/1.73 m<sup>2</sup>.
- 3. Patient with a tumor in solitary kidney.
- 4. Patient with bilateral or multiple renal tumors.
- 5. Contralateral unhealthy kidney.
- 6. Obese patients (BMI >30 Kg/M<sup>2</sup>)
- 7. Pregnant patient.
- 8. Patient refusing consent.
- 9. Patient missing or dead during follow up.

<u>Sample size:</u> Thus, 23 patients will be needed in each group (52).

<u>Sampling</u> <u>technique</u>: Purposive sampling technique will be applied to collect the sample for this study who are admitted with the diagnosis of renal cell carcinoma in the department of urology, BSMMU and Comfort nursing home (Pvt.) Ltd in Dhaka are selected as per inclusion and exclusion criteria for the present study. After written informed consent, total 52 patients are recruited and divided into two groups by lottery method.

<u>Study groups:</u> There are two groups of study subjects.

<u>Group-A:</u> Patients who were undergone partial nephrectomy by open method.

<u>Group-B:</u> Patients who were undergone radical nephrectomy by open method.

## **Pre-operative variable:**

- BMI of the patient
- Chronic disease/ co-morbid disease-cardiovascular (HTN), DM.
- Serum creatinine (mg/dl)
- eGFR (ml/min/1.93m<sup>2</sup>)

## <u>Post-operative Variable (outcome Variable):</u>

- Serum creatinine (mg/dl)
- eGFR (ml/min/1.73 m<sup>2</sup>)

## **Investigation**

## Diagnostic purpose:

- USG of whole abdomen.
- Computed tomography scan with urogram and angiogram.

## **Evaluation purpose:**

- Blood Hemoglobin level
- Urine R/M/E and C/S
- Serum electrolytes
- RBS
- CXR-P/A
- Serum Creatinine.
- eGFR

## Key steps of the procedure:

- Patient was included in the study after fulfilling the selection criteria (inclusion and exclusion criteria).
- Informed written consent was taken by all patients after explaining about the study, different management options, the possibility of response and the complications related to the procedure.
- Preoperative general fitness of the patients was checked by physical examinations and investigations.
- Under standard procedure, partial nephrectomy in group-A patients and radical nephrectomy in group-B patients were performed.

## Immediate postoperative follow up:

In this study, patients were followed up early 1,3,7 days postoperatively by evaluating-

Subjective complaints (History)



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- Clinical examination
- Investigation
  - o Urine R/M/E and C/S
  - Hemoglobin level
  - o Serum creatinine
  - o eGFR

## Subsequent follow up: 3 monthly for 1 year.

- History
- Clinical examination
- Investigation
  - o Urine R/M/E and C/S
  - o Hemoglobin level
  - Serum creatinine
  - eGFR

#### Date collection:

- The study subjects were selected on the basis of inclusion criteria from the patients who underwent partial nephrectomy or radical nephrectomy in the Department of Urology, BSMMU and Comfort nursing home (Pvt.) Ltd in Dhaka.
- The demographic information, relevant medical history, examination findings and investigation reports of all the study subjects were recorded in the data collection sheet.
- Any patient facing complications during the procedure was excluded from study.
- Any patient who died during follow up was excluded.
- All patients were conducted over telephone as scheduled for follow up after initial treatment.
- The data sheet was filled up after taking brief history, review of records and variable documents form patients.

#### Data analysis:

- After compilation, the data was presented in the form of tables, figures and graphs, as necessary.
- Statistical analysis of the results was done by using computer based statistical software SPSS 20.0 version for windows operating system.
- Results are expressed as mean (±SD) and compared by Student's unpaired (independent) and paired (dependent) t-test for continuous variables and Chi square test for categorical variables.
- A `p' value of < 0.05 was considered as significant.

### **Operational definition:**

**Renal cell carcinoma:** Renal cell carcinoma (RCC) is a kidney cancer that originates in the lining of the proximal convoluted tubule, a part of the very small tubes in the kidney that transport waste molecules from the blood to the urine.

**Radical nephrectomy:** The prototypical concept of RN encompasses the basic principles of early ligation of the renal artery and vein, removal of the kidney with primary dissection extremely to the Gerota fascia, excision of the ipsilateral adrenal gland, and performance of an extended lymphadenectomy form the crus of the diaphragm to the aortic bifurcation.

**Partial nephrectomy:** An operation to remove a kidney tumor by removing only part of the kidney leaving healthy tissue.

**Creatinine:** It is a breakdown product of creatinine phosphate in muscle and



is usually produced at a fairly constant rate by the body and excreted by kidneys in urine. The normal serum creatinine range for men is 0.6-1.3 mg/dL. The normal range for women is 0.5-1.2 mg/dl (Source: BSMMU biochemistry report, 2020).

Chronic kidney disease: Chronic kidney disease (CKD) is a progressive loss in kidney function over a period of months or years.

**Endophytic tumor:** An endophytic tumor was defined as less than 40% of the lesion extending off the surface of the kidney.

**Exophytictumor:** Tumor that intending to grow outward beyond the surface epithelium from which it originates.

Hypertension: Medical guidelines define hypertension as a blood pressure higher than 130 over 80 millimeters of mercury (mmHg), according to guidelines issued by the American Heart Association (AHA) in November 2017.

**Diabetes:** A disease in which the body's ability to produce or respond to the hormone insulin is impaired, resulting in abnormal metabolism of carbohydrates and elevated levels of glucose in when fasting. Less than 7.8 mmol/(140mg/dl) 2 hours after eating. In diabetes patient, blood sugar level in fasting condition-≤ 7.0 mmol/1, 2 hours after breakfast≥ 11.1 mmol/1 (Source: BSMMU biochemistry report, 2020).

**Kidney tumor:** Renal cell carcinoma is the commonest solid lesion within the kidney which originates form the proximal renal tubular epithelium and comprises different RCC types with specific histopathological and genetic characteristics,<sup>[7]</sup> From a clinical point of view. Three main types of RCC are important: clear cell (cRCC) 65%, papillary (pRCC-type I and II) 15% and chromophobe (chRCC) 10% generally, in all RCC types, prognosis worsens with stage and histopathological grade. Etiological factors include lifestyle such as smoking, obesity, hypertension and occupational exposure to specific carcinogens.[8] The 5-year overall survival for all types of RCC is 49%, which has further improved since 2006 probably due to an increase in incidentally detected RCCs as well as by the introduction of tyrosine kinase inhibitors. Sarcomatoid changes can be found in all RCC types and they are equivalent of high grade and very aggressive tumors.<sup>[9]</sup>

nephrectomy: Radical Radical refers nephrectomy complete removal of the kidney outside the Gerota fascia together with ipsilateral adrenal gland and complete regional lymphadenectomy from the crus of the diaphragm to the aortic bifurcation.[10]Radical nephrectomy is reserved for renal tumors that are not nephrectomy. amenable to partial Indication for radical nephrectomy nonfunctional include tumors in kidneys, large tumours replacing the majority of renal parenchyma, tumours associated with detectable regional lymphadenopathy, tumors or associated with renal vein thrombus. Complication relating to RN includes Suprahilar damage during and Retrocrural lymphadenectomy-



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duodenum, pancreas, liver, spleen, superior mesenteric artery, celiac trunk, superior mesenteric autonomic plexus, and cisterna chili, Injury to the vasculature of the Gut. There are two surgical approach for radical surgery-Flank approaches (Subcostal flank approach, Supracostalflank approach, Dorsallumbotomyapproach,

Thoracoabdominalapproach), Anterior approaches (Anterior midline approach, Anterior subcostal approach, Chevron incision, Bilateral anterior subcostal approach.<sup>[2]</sup>

**Partial** Nephrectomy: **Partial** nephrectomy is the surgical removal of a kidney tumor along with a thin rim of normal kidney, with the aims of curing the cancer and preserving as much normal kidney as possible. Whenever preservation of functioning parenchyma is important, partial nephrectomy substitutes for radical nephrectomy. The first partial nephrectomy was performed in 1884 by Wells for the removal of a perirenal fibro-lipoma [11]. Partial nephrectomy to treat renal malignancy was first described in 1890 by Czerny [12]. In Vermooten reported 1950, peripherally located. encapsulated renal tumors could be removed by partial excision of renal tissue Partial nephrectomy has now become a standard procedure for appropriately selected patients with renal carcinoma (RCC). Partial nephrectomy is indicated for cases in which a radical nephrectomy would render the patient a nephric with a subsequent immediate need for dialysis. Such cases include Synchronous bilateral RCC, Tumors in

a solitary kidney, Unilateral tumor with poorly functioning opposite kidney(imperative indications), Unilateral RCC and those with a functioning opposite kidney with an uncertain future function in artery hydronephrosis, chronic stenosis, pyelonephritis and systemic diseases such as diabetes and hypertension that result in arteriosclerosis and nephronimpairment, affecting elective indication patients with small (4 cm or less in diameter) unilateral tumors with a healthy contralateral organ.<sup>[13]</sup> Several surgical techniques are available for performing partial nephrectomy in patients with renal tumors. Description techniques, these including performing the incision, exposing the Kidneys, and closing the situs, are described in detail elsewhere.[14] The five main surgical processes include performing the incision, exposing the kidney, and closing the situs, are described in detail elsewhere (Monite JE and Novick AC, 1998). The five main surgical processes include enucleation of tissue, polar segmental nephrectomy, wedge resection, major transverse resection, and extracorporeal partial nephrectomy followed by renal autotransplantation,[13] of A11 these techniques require steady vascular control and thorough hemostasis, avoidance of renal ischemia, complete tumour removal with free margins, and efficient closure of the intrarenal collecting system. Finally, an adequate postoperative renal function must be maintained since a functioning renal remnant of at least 20% of one normal kidney is necessary to avoid end-stage renal failure.<sup>[15]</sup> However,



important not to compromise the extent of the surgical procedure to preserve renal function at the expense of an incomplete resection.

Estimated GFR: Glomerular filtration rate (GFR) is accepted as the best overall measure of kidney function. Measuring GFR directly is considered the most accurate way to detect changes in kidney status, but measuring the **GFR** directly complicated, requires experienced personnel, and is typically performed only in research settings and transplant centers.[16] The GFR can be estimated from serum creatinine concentration and demographic and clinical variables such as age, sex, ethnicity, and body size. Creatinine is a muscle waste product that is filtered form the blood by the Kidneys and released into the urine at a relatively steady rate. When function decreases. kidney less creatinine is eliminated and concentrations increases in the blood. With the creatinine test, a reasonable estimate of the actual GFR can be determined but not the accurate result. The normal mean value for GFR in healthy young men and women is approximately 130mL/min per 1.73 m<sup>2</sup>, per 120mL/min  $1.73m^{2}$ and respectively, declines and by approximately 1 mL/min per 1.73m<sup>2</sup> per year after 40 years of age [17]. For men, the equation of  $(ml/min/1.73m^2) = 194 \times (SCr)^{1.094} X$ (age) 0.287 and for women it is multiplied by 0.739. GFR is related to chronic kidney disease (CKD). Current guidelines define chronic kidney

disease kidney damage as or glomerular filtration rate (GFR) less than 60 mL/min per 1.73 m<sup>2</sup> for 3 months or more, regardless of cause.[18] To facilitate detection of chronic kidney disease. guidelines recommend different equations to calculate eGFR. The following two are most common and require a person's blood creatinine result, age, and assigned values based upon sex and race. Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation (2009) recommended by the National Kidney Foundation for calculating eGFR in adults. Modification of Diet in Renal disease Study (MDRD) equation which is now widely accepted and many clinical laboratories are using it to report GFR estimates.<sup>[19,20]</sup>

#### **RESULTS**

Distribution of patients by gender show [Table 1], most of the patients in both groups are male. In group A 14 (60.9%) patients are male and 09 (39.1%) patients are female. In group-B, 15(65.2%) patients are male 8(34.8%) patients are female (table-I), Mean (±SD) and range of distribution of the patients in group -A is 48.91±8.79 years, (35-65) years and in group-B is  $50.70 \pm 12.23$  years, (35-74) years (table-1), Mean (±SD) BMI in group-A is 20.70±2.36 kg/m2 and in group-B is  $21.22\pm6.36$  kg/m<sup>2</sup> (table-I). There are no statistically significant differences in demographic characteristic (sex, age) and BMI between two groups (p=0.760, 0.573, 0.714 respectively: [Table 1].



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Table 1: Patient's characteristics in both groups (n=46)

	Group-A	Group-B	P-Value
	(Partial nephrectomy)(n=23)	(Radical nephrectomy) (n=23)	
Sex			
Male	14(60.9)	15 (65.2)	0.760
Female	9(39.1)	8 (34.8)	
Age (years)			
(mean ± SD)	48.91 ± 8.79	5.70 ± 12.23	0.573
Range (years)	35-65	35-74	
BMI (kg/m2)	20.70±2.36	21.22±6.36	0.714
(mean±SD)			
Chi square test and independent't test was done to measure the level of significance			

Table 2: Pre- and post-operative symptoms & sign of the patients in both groups (n=46)

	Group-A	Group-B	P-Value
	(Partial	(Radical nephrectomy)	
	nephrectomy)(n=23)	(n=23)	
Pre-operative	-		
Flank pain			
Yes	18(78.3)	16(69.6)	0.502
No	5 (21.7)	7 (30.4)	
Hematuria			
Yes	5 (21.7)	7 (30.4)	0.502
No	18 (78.3)	16 (69.6)	
Diabetes			
Yes	6 (26.1)	5 (21.7)	0.730
No	17 (73.9)	18 (78.3)	
Hypertension			
Yes	10 (43.5)	10 (43.5)	1.000
No	13 (56.5)	13 (56.5)	
Post-Operative			
Fever			
Yes	3 (13.0)	2 (8.69)	1.000
No	20 (87.0)	21 (91.30)	

Chi-square test was done to measure the level of significance.

Table 3: Distribution of the patients according to tumor characteristics in both groups (n-46)

	Group-A	Group-B	P-Value
	(Partial	(Radical nephrectomy)	
	nephrectomy)(n=23)	(n=23)	
Tumor size (cm)	$4.28 \pm 0.91$	5.08 ± 0.89	0.004
Ranger (cm)	(2.60 - 6.30)	(2.90-6.90)	
Tumor location			
Upper pole	9 (39.1)	12 (52.2)	0.563



Lower pole	10 (43.5)	9 (39.1)	
Interpolar	4 (17.4)	2 (8.7)	
Tumor type			
Exophytic	19 (82.6)	5 (21.7)	0.013
Endophytic	4 (17.4)	18 (78.3)	
Hydronephrosis			
Yes	1 (4.3)	2 (8.6)	0.187
No	22 (95.7)	21 (91.3)	
Enhancement			
Yes	23 (100.0)	21 (91.3)	0.489
No	0 (0.0)	2 (8.7)	
Independent' t' test and Chi-square test was done to measure the level of significance			

Table 4: Serum creatinine status before and time depended changes after operation (at different follow up) in both groups (n=46)

Serum creatinine	Group-A	Group-B	P-
			Value
	(Partial nephrectomy) (n=23)	(Radical nephrectomy) (n=23)	
Before operation	$1.02 \pm 0.24$	$1.07 \pm 0.22$	0.432
After Operation			
At 1st POD	$1.23 \pm 0.28$	$1.34 \pm 0.35$	0.236
At 3rd POD	$1.17 \pm 0.25$	$1.32 \pm 0.29$	0.067
At 7th POD	$1.16 \pm 0.19$	$1.29 \pm 0.29$	0.087
After 3 months of POD	$1.11 \pm 0.23$	$1.35 \pm 0.27$	0.002
After 6 months of POD	$1.14 \pm 0.17$	$1.33 \pm 0.21$	0.002
After 9 months of POD	$1.13 \pm 0.16$	$1.37 \pm 0.20$	< 0.001
After 12 months of POD	$1.13 \pm 0.16$	$1.38 \pm 0.18$	< 0.001
Serum creatinine changes (before	$0.11 \pm 0.08$	$.31 \pm 0.04$	< 0.001
op vs after 12 months of POD)			
p-value (before op vs after12	0.002	0.003	
months of POD)			

Independent 't' test was done between groups and dependent't' test was done within group to measure the level of significance.

Table 5: eGFR status before and time depended changes after operation (at different follow up) in both groups (n=46)

eGFR	Group-A	Group-B	P-Value
	(Partial	(Radical	
	nephrectomy)(n=23)	nephrectomy)(n=23)	
Before operation	75.22 ± 14.48	73.17±17.74	0.671
After operation			
At 1st POD	64.39 ± 16.05	57.78 ± 11.50	0.116
At 3rd POD	67.52 ± 15.24	57.43 ± 10.23	0.012
At 7th POD	67.96 ± 13.66	60.13 ± 13.08	0.053
After 3 months of	69.65 ± 14.81	56.61 ± 11.58	0.002



POD			
After 6 months of	68.39 ± 13.61	55.91 ± 9.49	0.001
POD			
After 9 months of	68.52 ±12.52	$54.83 \pm 10.44$	<0.001
POD			
After 12 months of	68.91 ± 12.86	54.61 ±10.86	<0.001
POD			
Decrease in eGFR	$6.31 \pm 1.62$	$18.56 \pm 6.88$	<0.001
(ml/min)			
p-value (before op vs	<0.001	0.001	<0.001
after 12 Months of			
POD			

Independent' t test was done between groups and dependent' t' test was done within group to measure the level of significance.

Pre- and post-operative symptoms & sign of the patients in both groups shows [Table 2], 18 (78.3%) and 16 (69.6%) of the patients are presented with flank pain at presentation in group-A and group-B respectively and rest of the patients have no flank pain [Table 2]. 5 (21.7%) and 7 (30.4%) of the patients present with hematuria at presentation in group-A and group-B respectively and rest of the patients have no hematuria [Table 2]. Most of the patients are free from diabetes which are 17 (73.9%) in group-A and 18 (78.3%) in group-B and rest of the patients have no diabetes [Table 2]. Hypertension in present in 10 (43.5%) of the patients in both groups and rest of the patients have no hypertensions (table-II). During post-operative period, most of the patients had no postoperative fever which are 20 (87.00%) in group-A, 21 (91.3%) in group-B and minorities of the patients have postoperative fever in both groups [Table 2]. There are no statistically significant differences in pre- and post-operative clinical symptoms and signs of the patients between two groups (p=0.502,

0.502, 0.730, 1,000, 1.000 respectively: [Table 2])

Tumor size of kidney of the patients shows [Table 3], mean (±SD) tumor size in group-A 4.28 (± 0.91), cm, range 2.6-6.30 cm and in group-B 5.08 (±0.89) cm, range 2.9-6.9cm [Table 5]. Most of the renal tumors are exophytic 19 (82.6%) and rest of the tumors are endophytic 4 (17.4%) In Group-A [Table 3], and in group-B, 5(21.7%) of renal tumors are exophytic and 18 (78.3%)endophytic [Table 5]. There statistically significant differences in tumor size and in tumor type between groups (p=0.004,respectively). In group-A, renal tumors are located in 9 (39.1%) of the patients in the upper pole, 10 (43.5%) in lower pole and (17.4%)in the interpolar[Table 3], In group-B, tumors located in 12 (52.2%) of the patients in the upper pole, 9 (39.1%) in the lower pole and (8.7%)2 interpolar[Table 3]. In majority of the patients had no hydronephrosis in the kidney a diagnosis which are group-A 22 (95.7%) group-B 21 (91.3%) and



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minorities of the patients have hydronephrosis[Table 3] in group-A all the tumors have contrast enhancement and in group-B 21 (91.3%) had contrast enhancement and 2 (8.7%) had no contrast enhancement [Table 3]. There statistically significant are no differences in tumor location, hydronephrosis and in tumor contrast enhancement between two groups (p=0.563., 0.187, 0.489 respectively, [Table 3]).

During evaluation of patient's serum creatinine status before operation shows [Table 4], mean (±SD) serum creatinine in group-A 1.02 ±0.24 mg/dl and in group-B  $1.07 \pm 0.22$  mg/dl [Table 4] but there is no significant difference preoperatively (p=0.432).operation, time depended After changes of serum creatinine status of the patients at 1st, 3rd and 7th POD in group-A,  $1.23 \pm 0.28$ ,  $1.17 \pm 0.25$ ,  $1.16 \pm$ 0.19 mg/dl and in group-B,  $1.34 \pm 0.35$ , 1.32 0.29, 1.29±0.29 mg/dl respectively [Table 4] but there are no significant differences creatinine status at 1st, 3rd and 7th POD between two groups (p=0.236, 0.067, 0.087 respectively; [Table 4]). At 3, 6, 9 and 12 months follow up period after operation, time depended mean (±SD) serum creatinine status changes in group-A,  $1.11 \pm 0.23$ ,  $1.14 \pm 0.17$ ,  $1.13 \pm$ 0.16 mg/dl and in group-B,  $1.35 \pm 0.27$ , 1.33±0.21, 1.37± 0.20, 1.38± 0.18 mg/dl respectively (table-IV) but statistically significant differences present in serum creatinine status in 3,6,9 and 12 months POD between significant differences present in serum creatinine status in 3, 6, 9 and 12 months POD between

significant differences present in serum creatinine status in 3,6,9 and 12 months POD between two groups p= 0.002, 0.002, <0.001, <0.001 respectively, [Table 4]. The mean (± SD) serum changes creatinine status 12 months preoperative to after operation in group-A,  $0.11 \pm 0.08$ mg/dl and in group-B 0.31± 0.04 mg/dl which shows statistically significant differences is serum creatinine status between and within the groups (p<0.001, 0.002, respectively, [Table 4]).

During evaluation of patient's eGFR status before operation shows [Table 5] mean (±SD) eGFR in group-A, 75.22 ± 14.48 ml/min and in group-B, 73.17± 17.74 ml/min [Table 5] but there are no significant differences preoperatively (p=0.671). After operation, the time depended changes of eGFR status of the patients at 1st POD in group-A, 64.39±16.05 ml/min and in group-B, 57.78 ± 11.50 ml/min [Table 5] but there are no significant differences in eGFR status at 1st POD between two groups (p=0.116, [Table 5]). At 3rd, 7th POD and 3, 6, 9, 12 months follow up period after operation, time depended mean (±SD) eGFR status changes in group-A, 67.52 ± 15.24, 67.96 ± 13.66,  $69.65 \pm 14.81$ ,  $68.39 \pm 13.61$ ,  $68.91 \pm 12.86$ ml/min and in group-B,  $57.43 \pm 10.23$ ,  $60.13 \pm 13.08$ ,  $56.61 \pm 11.58$ ,  $55.91 \pm 9.49$ ,  $54.83 \pm 10.44$ ,  $54.61 \pm 10.86$  ml/min respectively; [Table 5]) but statistically significant differences present in eGFR status in 3rd, 7th POD and 3, 6, 9, 12 months follow up between two groups ('p' value in 3rd, 7th, 3, 6, 9 and 12 months POD = 0.012, 0.053, 0.002, 0.001,



<0.001 respectively; [Table 5]). The mean (±SD) eGFR status decreased from preoperative to 12 months after operation in group-A 6.31±1.62 ml/min and in group-B 18.56±6.88 ml/min which shows statistically significant differences in eGFR status from preoperative to 12 months follow up between and within the groups (p<0.001, <0.001, 0.001 respectively; [Table 5])</p>

#### **DISCUSSION**

With evolution of imaging modalities (USG, CT/MRI), small asymptomatic RCC is early diagnosed and the functional and oncological outcome of PN have increased. there is Currently, controversy regarding the clinical efficacy of PN and RN in treating localized RCC. According to EAU guideline (2014), nephrectomy is Partial the first treatment option for cTla tumor (<4 cm) and a viable option for cTlb lesion (>4cm) when technically feasible.[21] In this prospective study, pre-operative and post-operative time dependent changes of renal function up to 12 months after PN (Group-A) and RN (Group-B) are assessed by measuring eGFR using MDRD formula as renal function tends to be overestimated by serum creatinine which affected by several factors affecting creatinine generation. Is this study, the risk factors for the development of new onset of CKD (eGFR<60 ml/min) after operation are observed but univariate multivariate logistic regression analysis to predict association with renal function is not done. With regard to patient baseline characteristics (age, sex, BMI) in the current study, no significant differences (p=0.760, 0.573, 0.714 respectively) are noted that can affect renal function, an interesting finding is that the age ranges in group-A, (35-65) years and in group B, (35-74) years but classically renal tumors occur in sixth and seventh decades of life. The early occurrence of tumors in the current study perhaps due to easier access or exposure to carcinogen (smoking, industrial chemicals) and more rapid diagnostic and therapeutic methods available currently; additionally, many patients diagnostic and therapeutic methods available currently; additionally, many patients are diagnosed incidentally during medical evaluation for other symptoms.<sup>[22]</sup> Although compensatory hypertrophy occurs in all age groups after nephrectomy due to increased renal plasma flow and more pronounce in <30 years of age, effective renal plasma flow is known to decrease with patient age resulting in decreased compensatory hypertrophy increased age and progressive deterioration of renal function. Most of the patients in both groups are male (PN=60.9%, RN=65.2%) that indicates renal cell carcinoma is more prevalence in male and similar result (PN=67.5%, RN+66%) was also reported al.<sup>[23]</sup> scosvrev The male et predominance in our country may be due to presence of increased risk factors male (cigarette smoking, profession in various chemical industries and exposure to toxins). Male patients had a significantly greater increase in effective renal



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flow plasma as well creatinine clearance than female patients at 1 week (p<0.005) and at 1 year (p<0.0001) nephrectomy due to hypertrophy compensatory than female.<sup>[24]</sup> In case of BMI, obese patients (>30kg/m2) are excluded from this study and the result is slightly differ (average 21 Vs 23 kg/m2) from study noted by Miyamoto et al.[6] because majority of study population are lowincome group and most of them are note overweight. In pre and postoperative symptoms & sign (flank pain, hematuria, diabetes, hypertension, post-operative fever) of the patients in both groups have no significant differences (p= 0.502, 0.502 0.730, 1.00 1.00 respectively) and do not influence renal function, Different results were observed by Patel et al.[35] in which flank pain 48% in Ochsner clinic and 50% in UCLA hospital that were lower than present study (in group-A 78.3%, group-B 69.6% respectively) because they are more diagnosed incidentally and may get immediate management for pain. Though hematuria is the late presentation but within this study. hematuria is higher in group-B than group-A (21.7% vs.30.4%) because most of the tumors are larger and endophytic in group-B which may involve the PCS and may causes hematuria 35% in St. Luke's Hospital, 40% Ochsner clinic and in Mayo clinic 32%. Minorities of patients in this study have hypertension and diabetes that are well controlled preoperatively, intraoperatively and postoperatively up to follow up period by measuring regular blood pressure with getting anti-hypertensive drugs, measuring

blood sugar level with giving short acting insulin, oral hypoglycemic agents and advice is given to control hypertension was reported 44% in PN, 60.8% in RN by Liss et al.[25] compared to 43.5% in both groups of current study due to their sedentary life styles and consumption of lipid rich food. Several conflicting studies examined the long-term effects for renal donation on the contralateral kidney. Anderson et al.[10] noted that renal donors might be at slightly increased risk for the development hypertension of secondary to chronic hyperfiltration after unilateral nephrectomy. Miller et al.<sup>[26]</sup> reported that 31% of the patients develop hypertension after nephrectomy but has no significant impact on renal function (p<0.05). In baseline tumor characteristics, mean tumor size differs according to type of surgery in which lagger tumor in (5.8)cm) group-B than group-A (4.28cm) which influence the renal function in the present study (p=0.004) because larger tumor reduces more functional renal parenchyma. Leivovich et al.<sup>[21]</sup> reported that 4 cm or smaller RCC showed better quality of life and less renal impairment for PN than for RN. Comparable result is observed from the study by Simon et al.<sup>[27]</sup> which reported that mean tumors size in PN was 3.63 cm and in RN 5.54 statistically and there was cm significant difference (p<0.001). Different results were also observed in several studies due to large sample size and early incidental diagnosis of tumors in which mean (SD) tumor type (central vs peripheral) had no impact no renal function (serum creatinine 1.43



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mg/dl in both groups) although PN in technically more difficult in centrally located lesions leading to longer ischemia times and increased incidence of collecting system injuries. Other tumor characteristics (tumor location, contrast enhancement, hydronephrosis) have been examined for their association with outcomes in patients with RCC but there are no statistically differences (p<0.05). significant group-A, lower polar tumors are more (43.5%) and in group-B, upper polar tumors are more (52.2%.) There is minimal difference in the current study from another study by Patel et al.[28] which showed that tumors were located 34% in upper pole, 34% in the lower pole and 9% in the mid portion, in general, it is accepted that renal tumor enhancement of >15 Hounsfield unties (HU) in CT is suggestive of a malignancy.<sup>[29]</sup> The CT enhances have shown a significant association with histological subtypes of renal cell cancer which heterogeneous enhancement pattern is seen in clearcell RCC compared withchromophobe and papillary RCCs.[30] In this study, all the tumors in group-A and 91.3% group-B have contrast tumors in enhancement and rest of the tumors have USG features of RCC but statistically no significant difference is present (p=0.489). In majority of the patients had no hydronephrosis in the kidney during diagnoses which are 95.7% in group-A and 91.3% in group-B. No study was reported relating to contrast enhancement, hydronephrosis and renal function. In pre-operative period, mean serum creatinine status in lower in group-A than in group-B (1.02

vs 1.07 mg/dl; [Table 4]) and have no significant difference (p=0.432). Different mean serum creatinine results (PN=0.83 mg/dl, RN = 0.82 mg/dl; p=0.985) in the study by Miyamoto et al and (PN=1.27 mg/dl, RN= 1.17 mg/dl, p<0.001) in the study by krebs et al.<sup>[31]</sup>, were seen due to large sample size. The lower serum creatinine level in the current study may be due to more functioning renal parenchyma and small tumor size in affected kidney of group-A than group-B.

After operation, time-dependent changes of serum creatinine status of the patients at 1st, 3rd and 7th POD are less pronounced in group-A than (figure-I) and have group-B significant differences in both groups (p>0.05) but at 3, 6, 9 and 12 months, the changes remain stable up to 12 months in group-A but increases gradually in group-B (figure-I) and have no significant differences in both groups (p>0.002). Similar result was documented by Miyamoto et al.[6] in post-operative serum creatinine level between two groups (PN=0.96 mg/dl, RN=1.24 mg/dl; p<0.001). From preoperative to 12 Months after operation, mean creatinine status changes is less in group-A (0.11 mg/dl) than group-B (0.31 mg/dl) and statistically significant differences in between and within the groups (p= 0.002, 0.003 respectively). Comparable result found by Clark et al.[32] in a Prospective study in which creatinine clearance dropped more RN (0.56 ml/min, 31.6%) than PN (0.09 ml/min, 6.1%) and p<0.001. Hakim and Ringden et al.[33] documented that the removal



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of one kidney from a patient with two normally functioning kidneys results in functional adaptation compensatory hypertrophy of the remaining kidney. Creatinine clearance increases to 70 to 75% of the preoperative creatinine clearance within several weeks post-operatively. Several studies have followed patients for more than 10 years after door nephrectomy and found that creatinine clearance remined stable. In pre-operative period, mean eGFR is more in group-A (75.22 ml/min) than in group-B (73.17 ml/min) due to small tumor size and more functioning renal parenchyma and have no significant difference (p>0.671.) Similar eGFR results were observed in the studies (71.4 vs 71.3 ml/min, p>0.05) by Miyamoto et al. (2012) and (80.2 vs. 78.2 vs. 78.2 ml/min; P>0.05) by pignot et al (2014). The time depended changes mean eGFR status at 1st POD is not significant (P=0.116) but at 3rd, 7th POD and 3,6, 9, 12 months, it becomes significant in both groups (P<0.05)) because of more residual functioning renal parenchyma present after PN. Comparable result is noted Mariusdottir al.[4] et which in significant differences was observed post-operatively and after 6 months (56 vs. 44 ml/min, p< 0.001; 59 vs. 45 ml/min; p<0.001). The mean eGFR decreased more significantly in group-B (18.56 ml/min) than group-A (6.31 ml/min) from pre-operative to 12 months after operation and have significant difference (p<0.001; [Table 5]). The current results differ from the study by miyamoto et al.[6] in which eGFR decrease by 9.27 ml/min in PN

and 25.1 ml/min (p<0.0002) in RN due to large tumor size is PN and large sample size (152 patients). The timedependent changes of eGFR after RN show plateau from initially and then gradually declining form the first postoperative day to the 12 postoperative months. In case of PN, a lowest eGFR is observing in post-1 and operative day gradually recovered to near pre-operative level for 12 months (Anderson et al.[24] reported that compensatory hypertrophy was completed I week after donor nephrectomy and Tanaka et al.[34] reported 2 to 4 weeks after RN. Krebs et al.<sup>[31]</sup> reported that eGFR in PN patients were higher than RN in postoperatively. The compensatory hypertrophy after donor nephrectomy has previously been believed to be beneficial but compensatory hyperfiltration due to arterial vasodilatation with increased flow and eventually proteinuria, azotemia and hypertension but does not lead to long term decrease in renal function.[24] At the end of discussion, the present study suggested than although compensatory hypertrophy occurs in the early postoperative day in RN than PN, renal functional outcome is more stable in PN than RN due to functioning residual renal parenchyma.

#### CONCLUSION

Time dependent changes of estimated glomerular filtration rate (eGFR) after partial nephrectomy (PN) is better than radical nephrectomy (RN) for renal cell carcinoma (RCC) in 12 months follow up period. PN has minimal impact on



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post-operative renal function measured by eGFR whereas RN is associated with significantly greater renal function decline. PN is therefore the better procedure for preservation of renal function.

## **Limitations of the study**

- 1.Small sample size
- 2.Lack of longer follow up (only 12 months)
- 3.Surgery is performed by multiples surgeons.
- 4. Associated risk factors are not evaluated by logistic regression analysis.
- 5.Patients with renal failure (eGFR<30ml/min), obese patients and pregnant women are not included in the present study.

#### Recommendations

Observing time depended changes of eGFR of the present study. It can be said that partial nephrectomy has preserved renal function more than radical nephrectomy. With this view in mind following recommendation are for consideration of future put researchers as well as relevant authority.

- 1. Regular practice of partial nephrectomy in patients with localized RCC in our country.
- 2. Large sample size should be taken for further study.
- 3. Longer follow up should be given.
- 4. Intervention should be done by single surgeon.
- 5. Meta-analysis for further evaluation of renal function.

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